Modulated electro-hyperthermia: Experience along the years...

Presentation from "Oncotherm in Italy" conference 2025.04.02.

Prof. Dr. Elisabeth Arrojo

Radiation Oncologist
Director of hyperthermia's department at University Hospital Marqués of Valdecilla in Santander, Sapin;
Medical Director and Founder of the Medical Institute of advanced Oncology (INMOA) and CNPC, Spain
Professor at Catholic University of Murcia (UCAM)

Citation

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https://www.youtube.com/watch?v=u92N727a_Nw&list=PLEaAiXVgvMsGMMHSufONT8E7zYBSSDNO4

Oncothermia Journal 37, September 2025., 59-92.
https://oncotherm.com/ArrojoE_2025_Oncotherm_in_Italy_20250402

Rome, April 2025

Modulated electrohyperthermia: Experience along the years...

Elisabeth Arrojo, MD, PhD

Radiation Oncologist

- Director of hyperthermia's department at University Hospital Marqués of Valdecilla in Santander, Spain.
- Medical Director and Founder of the Medical Institute of advanced Oncology (INMOA) and CNPC, Spain
- Professor at Catholic University of Murcia (UCAM)

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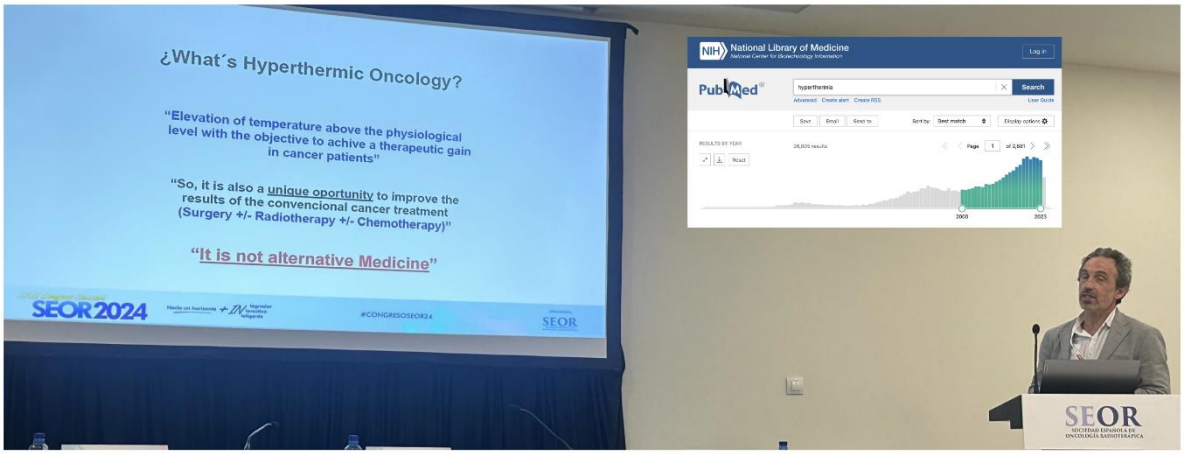
Valdecilla · INMOA · UCAM Universidad Católica de Murcia · CNPC

- European award of medicine.
- "Person of extraordinary abilities on sciences" by USA.

Spanish Radiation Oncology Society meeting - SEOR 2024



CNC HACIA EL FUTURO 2022 DE LA MANO DEL PACIENTE

GOBIERNO DE ESPAÑA · MINISTERIO DE LA PRESIDENCIA, RELACIONES CON LAS CORTES Y MEMORIA DEMOCRÁTICA

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Está Vd. en › Inicio › Buscar › Documento BOE-A-2006-17950

Orden SCO/3142/2006, de 20 de septiembre, por la que se aprueba y publica el programa formativo de la especialidad de Oncología Radioterápica.

DE LOS INMIGRANTES

MINISTERIO
DE SANIDAD Y CONSUMO

17950 *ORDEN SCO/3142/2006, de 20 de septiembre, por la que se aprueba y publica el programa formativo de la especialidad de Oncología Radioterápica.*

El artículo 21 de la Ley 44/2003, de 21 de noviembre, de ordenación de las profesiones sanitarias, establece el procedimiento para aprobar los programas formativos de las especialidades sanitarias en ciencias de la salud, previendo su publicación en el Boletín Oficial del Estado para general conocimiento.

La Comisión Nacional de la Especialidad de Oncología Radioterápica ha elaborado el programa formativo de dicha especialidad que ha sido

Disposición final.

Esta Orden entrará en vigor
«Boletín Oficial del Estado».

Madrid, 20 de septiembre de
Elena Salgado Méndez.

PROGRAMA OFICIAL DE L
RAD

Denominación oficial de la especialidad y requisitos de titulación

Oncología radioterápica.
Duración: 4 años.
Licenciatura previa: Medicina.

2.1.26.2 Hipertermia e irradiación:

Efectos biológicos de la hipertermia.
Termotolerancia.
Interacción radiación-hipertermia.
Indicaciones de la hipertermia en la radioterapia del cáncer.


Grupo Hipertermia SEOR
SEOR
Inicio
El Grupo
Hipertermia
Contacto
hipertermia@seor.es
Potenciando el tratamiento contra el cáncer
Hipertermia oncológica
El cuarto pilar en el tratamiento contra el cáncer
Uso
La hipertermia es un potenciador potente de tratamientos de radioterapia/quimioterapia
Inhibe la reparación del ADN
Potencia la expresión de antígenos
Reduce las zonas hipóxicas
Aumenta la permeabilidad de la membrana
Potencia el efecto abscopal
Y más beneficios Vea más >>
Evidencia científica
Patologías con nivel de evidencia IA y grado de recomendación A
Colorrectal avanzado
Mama locorregional avanzado/recidivante
Cérvix en tratamiento QT/RT
Sarcoma de partes blandas
Recidivas cutáneas
Cabeza y cuello avanzado Vea más >>
Valdecilla
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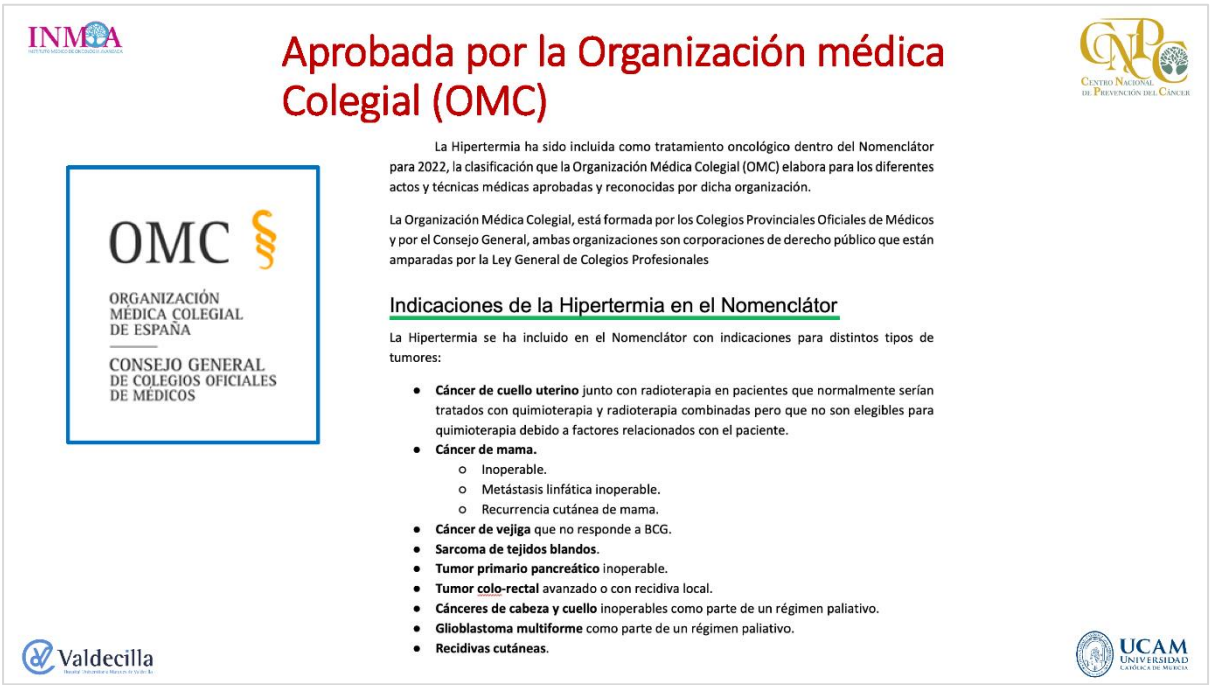
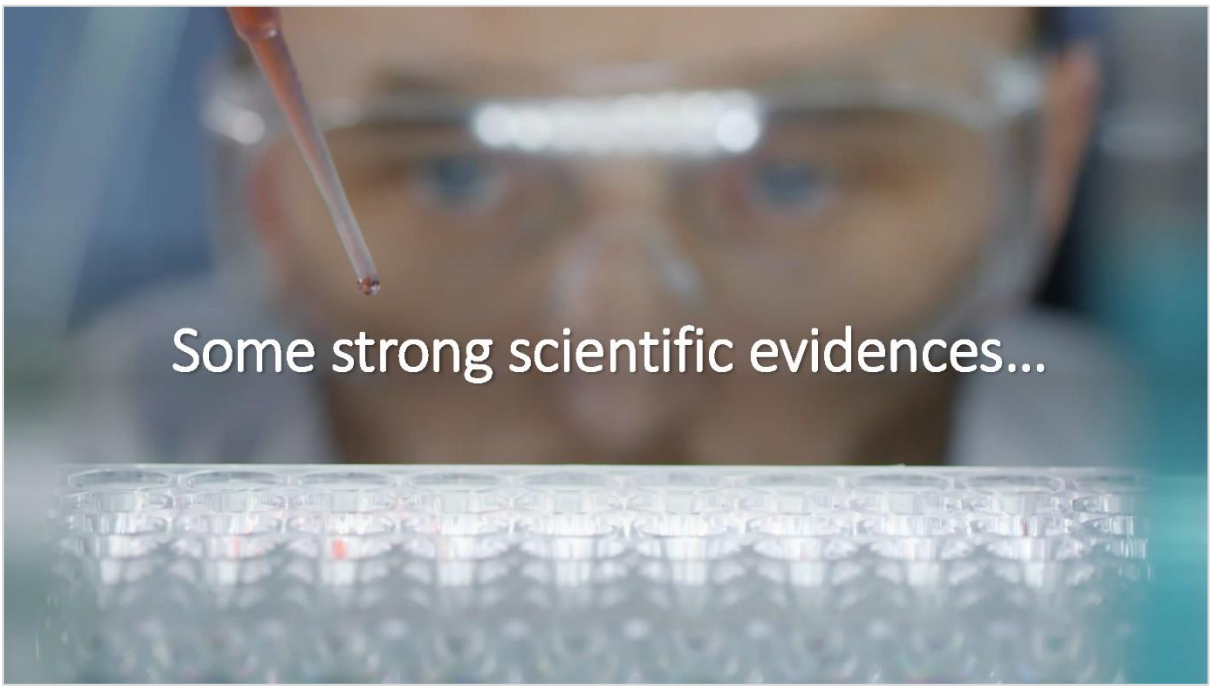

Aprobada por la Organización médica Colegial (OMC)
OMC
ORGANIZACIÓN MÉDICA COLEGIAL DE ESPAÑA
CONSEJO GENERAL DE COLEGIOS OFICIALES DE MÉDICOS
La Hipertermia ha sido incluida como tratamiento oncológico dentro del Nomenclátor para 2022, la clasificación que la Organización Médica Colegial (OMC) elabora para los diferentes actos y técnicas médicas aprobadas y reconocidas por dicha organización.
La Organización Médica Colegial, está formada por los Colegios Provinciales Oficiales de Médicos y por el Consejo General, ambas organizaciones son corporaciones de derecho público que están amparadas por la Ley General de Colegios Profesionales
Indicaciones de la Hipertermia en el Nomenclátor
La Hipertermia se ha incluido en el Nomenclátor con indicaciones para distintos tipos de tumores:
Cáncer de cuello uterino junto con radioterapia en pacientes que normalmente serían tratados con quimioterapia y radioterapia combinadas pero que no son elegibles para quimioterapia debido a factores relacionados con el paciente.
Cáncer de mama.
Inoperable.
Metástasis linfática inoperable.
Recurrencia cutánea de mama.
Cáncer de vejiga que no responde a BCG.
Sarcoma de tejidos blandos.
Tumor primario pancreático inoperable.
Tumor colo-rectal avanzado o con recidiva local.
Cánceres de cabeza y cuello inoperables como parte de un régimen paliativo.
Glioblastoma multiforme como parte de un régimen paliativo.
Recidivas cutáneas.
Valdecilla
UCAM



JAMA Oncol. 2018;4(4):483-492.
doi:10.1001/jamaoncol.2017.4996

JAMA Oncology | Original Investigation

Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia on Long-term Outcomes Among Patients With Localized High-Risk Soft Tissue Sarcoma
The EORTC 62961-ESHO 95 Randomized Clinical Trial

- Phase 3 randomized clinical trial
- Germany (6), Norway (1), Austria (1), and the United States (1).
- Ages 18 - 70 years.
- Histologically proven **soft tissue sarcoma** with the following risk criteria:
  - Tumor diameter ≥ 5 cm or larger.
  - Grade 2 or 3.
  - Deep to the fascia.
  - No evidence of distant metastases.
- **Objectives:**
  - **Primary:** Local progression-free survival.
  - **Secondary:**
    - Tumor response to induction therapy.
    - Disease-free survival.
    - Survival.

9 HYPERTHERMIA CENTERS

EUROPE:
- University Hospital Munich-Grosshadern of the LMU
- Argirov Clinic Starnberger See
- Rotkreuz Krankenhaus Munich
- Essen University Hospital
- Düsseldorf University Hospital
- Charité – Universitätsmedizin Berlin
- University Hospital Graz
- Haukeland University Hospital, Bergen

USA:
- Duke University Hospital, Durham

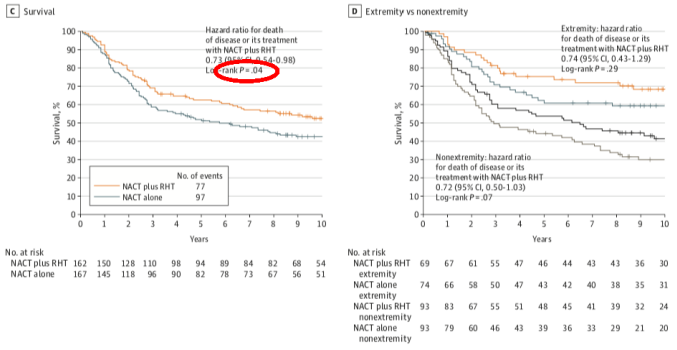
The median follow-up duration was 11.3 (9.2-14.7) years.

OS HT+CT vs CT:

- 5 years:
  62.7% vs 51.3%,
  (p = 0.04)

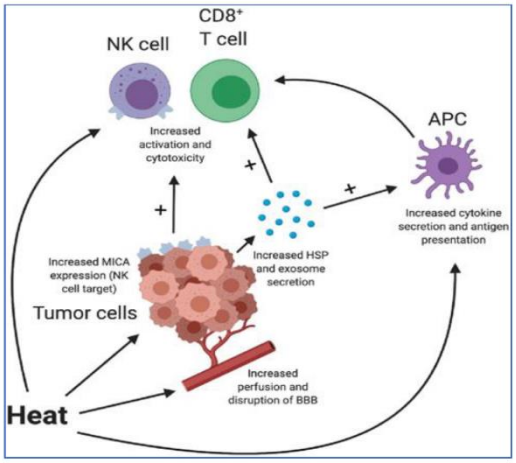
JAMA Oncology | Original Investigation

Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia on Long-term Outcomes Among Patients With Localized High-Risk Soft Tissue Sarcoma
The EORTC 62961-ESHO 95 Randomized Clinical Trial



A, Median local progression free survival was 5.6 years (95% CI, 2.9-8.7) in the NACT plus RHT group compared with 2.4 years (95% CI, 1.7-4.2) in the NACT-alone group. B, Median disease-free survival was 2.8 years (95% CI, 2.0-4.9) in the NACT plus RHT group compared with 1.5 years (95% CI, 1.1-2.1) in the NACT-alone group. C, Median survival was 15.4 years (95% CI, 6.6 to >17.0 [the upper confidence limit cannot be estimated and represents the lower bound for the value to be expected]) in the NACT plus RHT group compared with 6.2 years (95% CI, 3.2-10.3) in the NACT-alone group. D, Extremity tumor-survival rates at 5 and 10 years were 75.2% and 68.3% in the NACT plus RHT group compared with 60.8% and 59.2% in the NACT-alone group. The absolute difference at 5 years was 14.4% (95% CI, 0%-29.5%) and was 9.1% (95% CI, 0%-24.7%) at 10 years. Nonextremity tumor-survival rates at 5 years and 10 years were 53.5% and 41.3% in the NACT plus RHT group compared with 44.0% and 29.9% in the NACT-alone group. The absolute difference at 5 years was 9.5% (95% CI, 0%-23.8%) and was 11.4% (95% CI, 0%-25.1%) at 10 years. NACT indicates neoadjuvant chemotherapy consisting of doxorubicin, ifosfamide, and etoposide; RHT, regional hyperthermia.

Hyperthermia estimulates immune system...



Srinivasan, et al. The intersection between immunotherapy and laser interstitial thermal therapy: a multipronged future of neuro-oncology. International Journal of Hyperthermia.

European Journal of Cancer 158 (2021) 123–132

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

Rolf D. Issels [a,*,1], Elfriede Noessner [b,1], Lars H. Lindner [a], Michael Schmidt [c], Markus Albertsmeier [d], Jean-Yves Blay [e], Emanuel Stutz [f], Yujun Xu [g], Veit Buecklein [a], Annelore Altendorf-Hofmann [h], Sultan Abdel-Rahman [a], Ulrich Mansmann [g], Michael von Bergwelt-Baildon [i], Thomas Knoesel [j]

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[b] Helmholtz Zentrum München, German Research Center for Environmental Health, Germany
[c] Munich Cancer Registry, Institute of Medical Information Processing, Biometry and Epidemiology, LMU, Munich, Germany
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[h] Department of General, Visceral and Vascular Surgery, University Hospital Jena, Germany
[i] Deutsches Konsortium für Translationale Krebsforschung, Bayrisches Zentrum für Krebsforschung, and Comprehensive Cancer Center LMU, Munich, Germany
[j] Institute of Pathology, LMU, Thalkirchner Str.36, Munich, 80337, Germany

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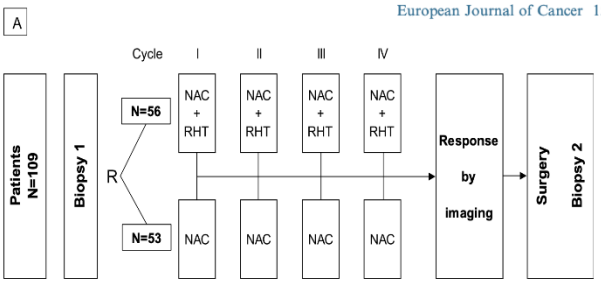
Available online 16 October 2021

- The study protocol included an optional accompanying **translational program, to determine immune cells of tumour tissue.**

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

European Journal of Cancer 158 (2021) 123–132



- **28 patients had paired samples** (only available for patients who had been biopsied and finally operated at the Munich Centre).
  - NAC-RHT: 13
  - NAC: 15

Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 rando

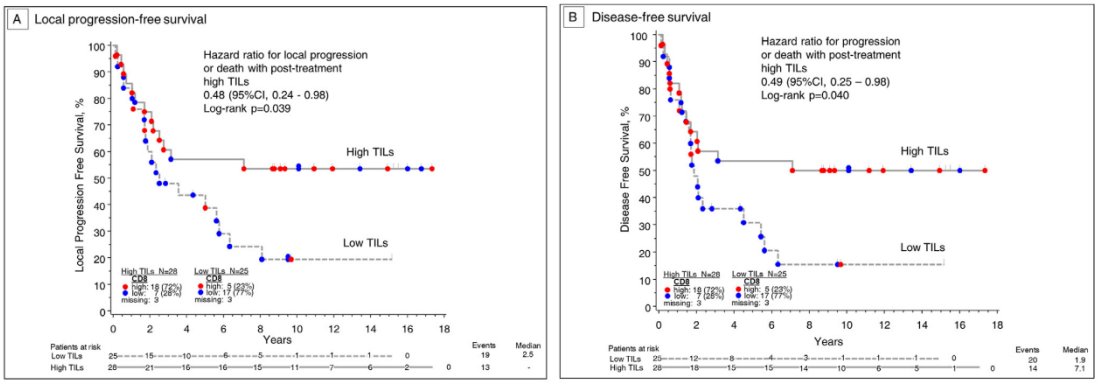
European Journal of Cancer 158 (2021) 123–132

- Examined for **TILs (Infiltrating tumor lymphocytes)** and immune biomarker expression, including **CD8, PD-1, PD-L1, and FOXP3.**
  - The TIL score was assigned as high (>5 cells per HPF) or low (5 cells per HPF).
  - The CD8 cell score was defined by anti-CD8 antibody immunoreactivity as high (>10 cells per HPF) or low (<10 cells per HPF)

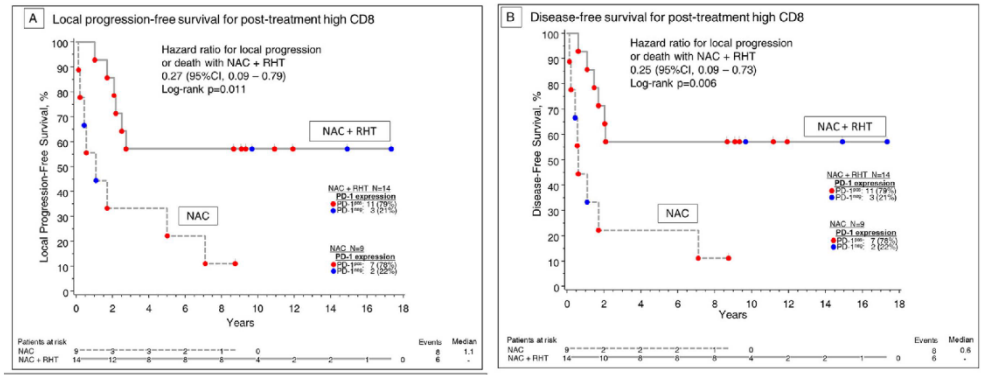
Immune infiltrates in patients with localised high-risk soft tissue sarcoma treated with neoadjuvant chemotherapy without or with regional hyperthermia: A translational research program of the EORTC 62961-ESHO 95 randomised clinical trial

European Journal of Cancer 158 (2021) 123–132

- In post-treatment samples (biopsy 2): **53%** (28/53) tumours **high TIL infiltrate** *vs* 47% (25/53) with low TIL infiltrate.
- **High TILs significantly associated with prolonged LPFS (p 0.039) and DFS (0.040)**



High CD8 by groups



Patients of the NAC-RHT group, whose tumours exhibited high CD8 counts, had significantly longer LPFS (p=0.011) and DFS (p =0.006) compared to the NAC group.

CONCLUSIONS

- **Preoperative chemotherapy +/- concomitant Hyperthermia turned the state of a cold, non-immunogenic sarcoma into a more immunogenic tumour** with high TILs, a decrease of immune-suppressive FOXP3 regulatory Tcells, and absence of PD-L1 expression.
- In patients with **high increase in CD8, the addition of hyperthermia significantly increased local progression free survival and disease free survival.**

Immune effect of hyperthermia

World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Clin Oncol 2021 November 24; 12(11): 1064-1071

DOI: 10.5306/wjco.v12.i11.1064

ISSN 2218-4333 (online)

ORIGINAL ARTICLE

Observational Study

Modulated electro-hyperthermia in stage III and IV pancreatic cancer: Results of an observational study on 158 patients

Giammaria Fiorentini, Donatella Sarti, Girolamo Ranieri, Cosmo Damiano Gadaleta, Caterina Milandri, Andrea Mambrini, Stefano Guadagni

INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY • BIOLOGY • PHYSICS ASTRO

CLINICAL INVESTIGATION | VOLUME 100, ISSUE 1, P78-87, JANUARY 01, 2018

Comparing the Effectiveness of Combined External Beam Radiation and Hyperthermia Versus External Beam Radiation Alone in Treating Patients With Painful Bony Metastases: A Phase 3 Prospective, Randomized, Controlled Trial

Mau-Shin Chi, MD • Kai-Lin Yang, MD • Yue-Cune Chang, PhD • ... Kuang-Wen Liao, PhD • Motoharu Kondo, MD, PhD • Kwan-Hwa Chi, MD • Show all authors

Purpose

To compare the response, duration of pain relief, and time to achieve complete pain relief after radiation therapy (RT) with o

for updates

Conclusions

The addition of HT to RT significantly increases the pain control rate and extends response duration compared with RT alone for painful bony metastases.

Results

The study was terminated early after an interim analysis of 57 patients, 3 years after the first enrollment (November 2013 to November 2016): 29 patients in the RT + HT group and 28 patients in the RT-alone group. The CR rate at 3 months after treatment was 37.9% in the RT + HT group versus 7.1% in the RT-alone group (P=.006). The accumulated CR rate within 3 months after treatment was 58.6% in the RT + HT group versus 32.1% in the RT-alone group (P=.045). Median time to pain progression was 55 days in patients with CR (n=9) in the RT-alone group, whereas the endpoint was not reached during the 24-week follow-up in the RT + HT group (P<.01).

Conclusions

The addition of HT to RT significantly increases the pain control rate and extends response duration compared with RT alone for painful bony metastases.

Radiotherapy and Oncology 138 (2019) 1–8

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

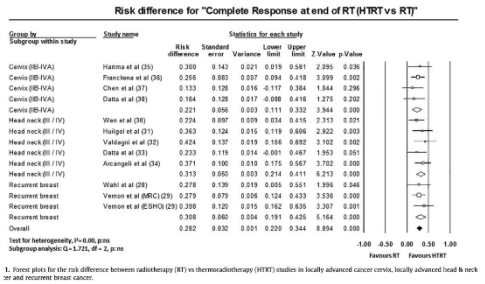
Original Article

Hyperthermia with radiotherapy reduces tumour alpha/beta: Insights from trials of thermoradiotherapy vs radiotherapy alone

Niloy R. Datta [a,*], Stephan Bodis [a,b]

[a] Centre for Radiation Oncology KSA-KSB, Kantonsspital Aarau; and [b] Department of Radiation Oncology, University Hospital Zurich, Switzerland

- Hyperthermia increase BED (biological equivalent dose in RT)
- Metaanalises randomized studies wtih radiotherapy vs radiotherapy + regional hyperthermia in:
  - Recurrent breast cancer
  - Locally advanced head and neck cancer
  - Locally advanced cervical cancer
- 12 stuides (show RT+HT significantly better in complete response than RT alone)
- Excluded those with different doses o dose fractionation



1. Forest plots for the risk difference between radiotherapy (RT) vs thermoradiotherapy (HTRT) studies in locally advanced cancer cervix, locally advanced head & neck cer and recurrent breast cancer.

Hyperthermia and BED

Table 1
Summary of the randomized studies of RT vs HTRT, complete responders in each arm, corresponding BED of the RT schedule and the estimated α/β with HTRT for each study.

Author	Site	RT/HTRT		Hyperthermia				RT			HTRT			BED (RT) ($Gy_{\alpha/\beta}$)	$\%CR_{HTRT}/\%CR_{RT}$ (%)	BED_{HTRT} (Gy)	Estimated α/β for HTRT (Gy)
		Dose (Gy)	Dose/fr (Gy)	T (°C)	Time (mins)	Per week	Total sessions	Total	CR		Total	CR					
Wahl et al. [35]	RcBC	48.0	2.0	NA	NA	NA	NA	18	7	39	24	57.6	1.71	98.7	1.89		
Vernon et al. (MRC) [36]	RcBC	28.8	3.6	43.0	60.0	1	3	59	17	90	51	39.2	1.97	77.0	2.15		
Vernon et al. (ESHO) [36]	RcBC	32.0	4.0	43.0	60.0	2	8	29	11	27	21	44.8	2.05	91.9	2.14		
Wen et al. [37]	LAHNC	70.0	2.0	44.4	60.0	2	6	49	23	49	34	84.0	1.48	124.2	2.58		
Huilgol et al. [38]	LAHNC	70.0	2.0	42.3	30.0	1	7	26	11	28	22	84.0	1.86	156.0	1.63		
Valdagni et al. [39]	LAHNC	68.0	2.0	42.5	30.0	2	12	22	9	18	15	81.6	2.04	165.0	1.38		
Datta et al. [40]	LAHNC	64.0	2.0	42.5	50.0	2	12	32	10	33	18	76.8	1.75	134.1	1.83		
Arcangeli et al. [41]	LAHNC	60.0	1.5	42.5	45.0	3	7	43	18	38	30	69.0	1.89	130.1	1.28		
Harima et al. [42]	LACC	52.2	1.8	40.6	60.0	1	3	20	10	20	16	61.6	1.60	98.6	2.03		
Franckena et al. [43]	LACC	48.3	2.0	42.0	60.0	1	5	56	32	58	48	58.0	1.45	83.9	2.71		
Chen et al. [44]	LACC	40.0	2.0	42.0	45.0	2	8	30	14	30	18	48.0	1.29	61.7	3.68		
Datta et al. [45]	LACC	60.0	2.0	42.5	45.0	2	12	26	15	27	20	72.0	1.28	92.4	3.70		

Abbreviations: RT: Radiotherapy; HTRT: Thermoradiotherapy; T: Temperature; RcBC: Recurrent breast cancer; LAHNC: Locally advanced head and neck cancer; LACC: Locally advanced cancer cervix; BED: Biologically effective dose; RcBC: Recurrent breast cancer; LAHNC: Locally advanced head and neck cancer; LACC: Locally advanced cancer cervix; $\%CR_{HTRT}$: % complete response with HTRT; $\%CR_{RT}$: % complete response with RT.
BED_{HTRT} and α/β_{HTRT} are estimated as described in text.
[a] Average dose to RT group: 68 Gy whilst to HTRT 67.5 Gy.
[b] Only patients with neck nodes were considered, treated with 1.5 Gy–2 Gy per fraction, 3 fractions/day.
For all LACC studies, only external RT doses were considered.

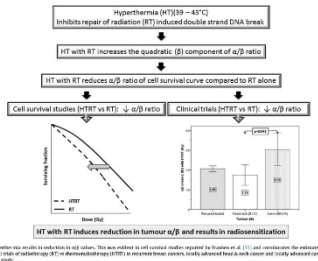
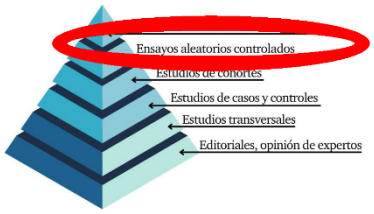


Fig. 4. Hyperther mia results in reduction in α/β values. This was evident in cell survival studies reported by Fyrodes et al. [9] and corroborates the estimated α/β values from clinical trials of radiotherapy (RT) vs thermoradiotherapy (HTRT) in recurrent breast cancers, locally advanced head & neck cancer and locally advanced cancer cervix in the present study.

BED

Tipo tumor	BED RT	BED RT + HT
Mama Recurrente	47.2Gy (39.2-57.6)	**89.2 Gy** (77.0-98.7)
HYN LA	79.1Gy (69-84)	**141.9Gy** (124.2–165.0)
Cérvix LA	59.9Gy (48-72)	**84.2Gy** (61.7–98.5)



Locally advanced rectal cancer

INTERNATIONAL JOURNAL OF HYPERTHERMIA
2021, VOL. 38, NO. 1, 144-151
https://doi.org/10.1080/02656736.2021.1877837

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Beneficial effects of modulated electro-hyperthermia during neoadjuvant treatment for locally advanced rectal cancer

Sunghyun Kim [a], Jun Hyeok Lee[b], Jihye Cha[a], and Sei Hwan You[a]

[a] Department of Radiation Oncology, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea [b] Department of Biostatistics, Yonsei University Wonju College of Medicine, Wonju, Korea

Valdecilla

MATERIALS AND METHODS Clinical data were analyzed for 120 patients who received neoadjuvant treatment for locally advanced rectal cancer (T3/4 or N+, M0) from May 2012 to December 2017. Capecitabine or 5-fluorouracil was administered along with radiotherapy. Patients were categorized into mEHT group (62 patients) and non-mEHT group (58 patients) depending on whether mEHT was added. Surgery was performed 6–8 weeks after the end of radiotherapy.

Table 1. Patient characteristics before neoadjuvant treatment. (Table view)

Characteristics	mEHT group ($n = 62$)	non-mEHT group ($n = 58$)	p value
Median age, yrs. (range)	59 (33–83)	57 (43–82)	.511
Sex, n			.300
Male	46 (74.2%)	38 (65.5%)	
Female	16 (25.8%)	20 (34.5%)	
Pathology, n			.160
Adenocarcinoma	59 (95.2%)	55 (94.8%)	
Mucinous adenocarcinoma	2 (3.2%)	3 (5.2%)	
Tubular adenocarcinoma	1 (1.6%)	0 (0.0%)	
Differentiation, n			.895
Well differentiated	10 (16.1%)	9 (15.5%)	
Moderate differentiated	48 (77.4%)	47 (81.0%)	
Poor differentiated	3 (4.8%)	1 (1.7%)	
Unknown	1 (1.6%)	1 (1.7%)	
Anal verge range, n			.379
<5cm	38 (61.3%)	41 (70.7%)	
≥5cm, <10cm	16 (25.8%)	9 (15.5%)	
≥10cm	8 (12.9%)	8 (13.8%)	
Initial clinical T stage, n			.887
cT2	2 (3.2%)	3 (5.2%)	
cT3	46 (74.2%)	43 (74.1%)	
cT4	14 (22.6%)	12 (20.7%)	
Initial clinical N stage, n			.052
cN0	0 (0%)	4 (6.9%)	
cN+	62 (100.0%)	54 (93.1%)	
Mean initial primary tumor volume, mL (± SD*)	62.6 (± 41.8)	61.9 (± 66.7)	.941

*SD: standard deviation.

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Table 2. Neoadjuvant treatment summary. (Table view)

Treatment	mEHT group ($n = 62$)	non-mERT group ($n = 58$)
Radiation dose, n (mEHT No. range)		
40 Gy	57 (8–9)	0
50.4 Gy	5* (1–12)	58
Chemotherapy regimen, *n*		
5-fluorouracil with leucovorin	6 (9.7%)	27 (46.6%)
Capecitabine	55 (88.7%)	31 (53.4%)
others	1 (1.6%)	0 (0%)
Type of resection, *n*		
Low anterior resection	53 (85.5%)	47 (81.0%)
Abdominoperineal resection	4 (6.5%)	9 (15.5%)
Others	5 (8.0%)	2 (3.5%)
Mean overall treatment time†, day (± SD‡)	80.2 (± 8.4)	90.9 (± 9.6)

*One of them had a radiation dose of 47.4 Gy, † Overall treatment time: Duration from first radiotherapy day to operation day. ‡SD: standard deviation.

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Table 3. Surgical pathology results. (Table view)

	mEHT group (n = 62)	non- mEHT group (n = 58)	*p* value
Pathologic T stage, *n*			.196
ypT0-is	13 (21.0%)	6 (10.4%)	
ypT1-2	21 (33.9%)	18 (31.0%)	
ypT3-4	28 (45.1%)	34 (58.6%)	
T-downstaging rate, n/all	41/62 (66.1%)	33/58 (56.9%)	.299
Pathologic N stage, *n*			.180
ypN0	50 (80.7%)	41 (70.7%)	
ypN+	12 (19.3%)	17 (29.3%)	
N-downstaging rate, n/all	56/62 (90.3%)	48/54† (88.9%)	.800
ypStage, n			.422
ypCR	11 (17.7%)	5 (8.6%)	
Stage 0 (ypTisN0)	1 (1.6%)	1 (1.7%)	
Stage I	18 (29.0%)	13 (22.4%)	
Stage II	20 (32.3%)	22 (38.0%)	
Stage III	12 (19.4%)	17 (29.3%)	
Downstaging rate, n/all	50/62 (80.7%)	39/58 (67.2%)	.094
Resection margin status, n/all (%)			.841
Negative	56 (90.3%)	53 (91.4%)	
Positive	6 (9.7%)	5 (8.6%)	
TRG*, *n*			.146
TRG1 (Minimal regression)	9 (14.5%)	8 (13.8%)	
TRG2 (Moderate regression)	31 (50.0%)	27 (46.6%)	
TRG3 (Near total regression)	10 (16.1%)	18 (31.0%)	
TRG4 (Total regression)	12 (19.4%)	5 (8.6%)	
Good TRG score, TRG 3 + 4/all	22/62 (35.5%)	23/58 (39.7%)	.637
Initial primary tumor volume <65 mL	16/43 (37.2%)	23/43 (53.5%)	.130
Initial primary tumor volume ≥65 mL	6/19 (31.6%)	0/15 (0%)	.024

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*TRG: Tumor regression grade. †Excluding 4 patients with icN0.

RESULTS

- The **median radiation dose was significantly less for mEHT group (40 Gy) than for non-mEHT group (50.4 Gy).**
  - In mEHT group, 80.7% showed down-staging compared with 67.2% in non-mEHT group.
  - For **large tumors of more than 65 cm³** (mean), **improved tumor regression was observed in 31.6% of mEHT group compared** with 0% of non-mEHT group **(*p* = .024).**
  - The **gastrointestinal toxicity rate of mEHT group was 64.5%,** which was found to be **statistically significantly less than 87.9% of non-mEHT group (*p* = .010).**
  - The 2-year disease-free survival was 96% for mEHT group and 79% for non-mEHT group (*p* = .054).

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CONCLUSIONS

- The **overall mEHT group had a comparable response and survival using less radiation dosing compared with standard care.**
- **The subgroup with large tumors showed significantly improved efficacy for tumor regression after mEHT.**
- **The mEHT group had significantly less GI toxicity.**

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cancers

MDPI

Systematic Review

Meta-Analysis of Modulated Electro-Hyperthermia and Tumor Treating Fields in the Treatment of Glioblastomas

Attila Marcell Szasz [1,*], Elisabeth Estefanía Arrojo Alvarez [2,3], Giammaria Fiorentini [4,5], Magdolna Herold [1,6], Zoltan Herold [1], Donatella Sarti [4] and Magdolna Dank [1]

[1] Division of Oncology, Department of Internal Medicine and Oncology, Semmelweis University, 1083 Budapest, Hungary
[2] Oncología Radioterápica, Servicios y Unidades Asistenciales, Hospital Universitario Marqués de Valdecilla, 39008 Santander, Spain
[3] Medical Institute of Advanced Oncology, 28037 Madrid, Spain
[4] Department of Oncology, Azienda Ospedaliera "Ospedali Riuniti Marche Nord", 61121 Pesaro, Italy
[5] IHF Integrative Oncology Outpatient Clinic, 40121 Bologna, Italy
[6] Department of Internal Medicine and Hematology, Semmelweis University, 1088 Budapest, Hungary
* Correspondence: szasz.attila_marcell@med.semmelweis-univ.hu; Tel.: +36-1-459-1500

Citation: Szasz, A.M.; Arrojo Alvarez E.E.; Fiorentini, G.; Herold, M.; Herold, Z.; Sarti, D.; Dank, M. Meta-Analysis of Modulated Electro-Hyperthermia and Tumor Treating Fields in the Treatment of Glioblastomas. *Cancers* **2023**, *15*, 880. https://doi.org/10.3390/cancers15030880

Received: 30 November 2022
Revised: 25 January 2023
Accepted: 29 January 2023
Published: 31 January 2023

Valdecilla INMA UCAM

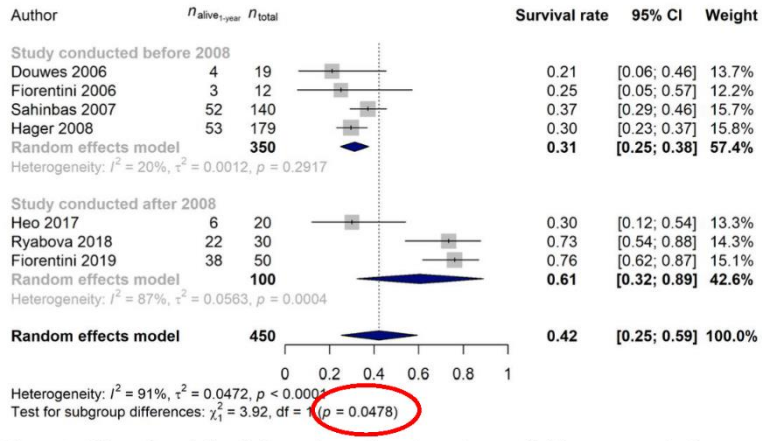

Figure 3. Effect of modulated electro-hyperthermia on 1-year glioblastoma survival rate, grouped by studies published before and after 2008 [43,46–51].

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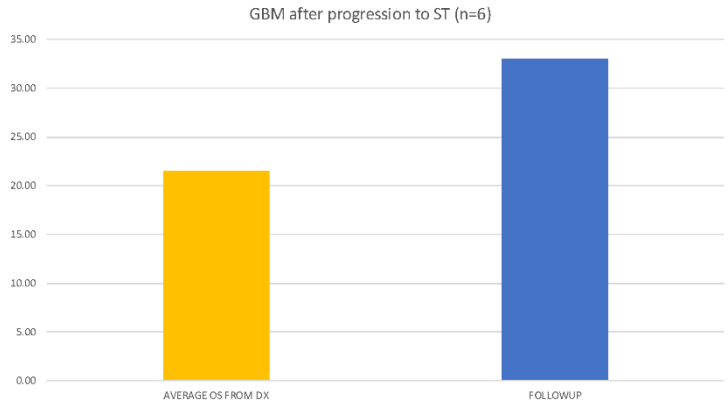
mEHT Glio Trial

Progression group: Analyzing the impact of adding mEHT to standard second line chemotherapy in patients with progression after ST for GBM.

- 6 patients were included (100% IDH negative).
- Average age was 54 years old (42-70).
- Second line chemotherapy was Fotemustine in 66.6%, Bevacizumab in 16.6% and Temozolamide in 16.6% of the cases.

Valdecilla UCAM Universidad Católica de Murcia INMOA Instituto Médico de Oncología Avanzada

mEHT Glio Trial



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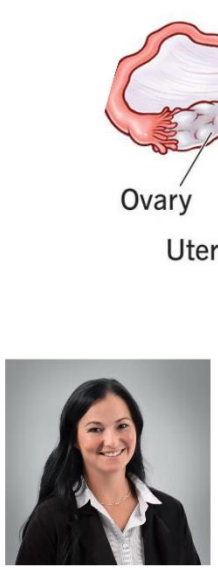
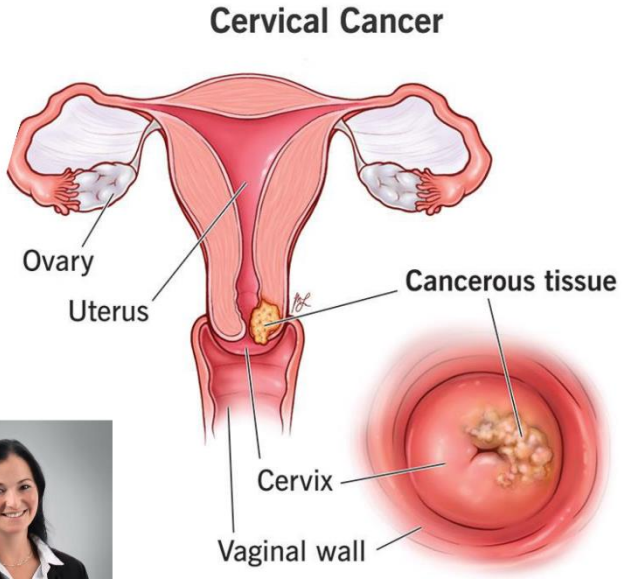
HT level I evidence (ESTRO)



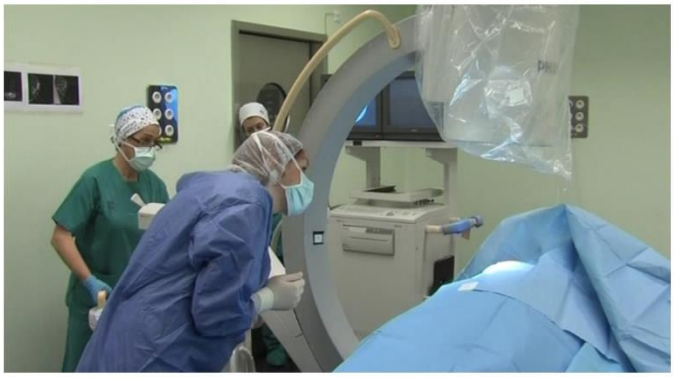
Dr. Carrie Minnaar



9 months after finishing my residency program....

Fuente: EFE, 31 de enero. 2014 12:37

El Hospital Valdecilla, en Santander, aplica en una sesión la radioterapia para cáncer de mama



Pioneer technique for breast cancer RT: From 6-7 weeks lenght to only 1 treatment of about 15 min

El gerente del Hospital, César Pascual, ha presentado hoy esta nueva técnica junto al jefe del Servicio de Oncología Radioterápica, Pedro Prada, y a la **médico adjunto que está al frente del proyecto, Elisabeth Arrojo.**

Valdecilla INMA UCAM

Research coordinatior

400 clinics in USA

Michigan USA

Valdecilla INMA UCAM

My mum…

- **Brain surgery June 2018**
- Radiosurgery
- 4 different types of immunotherapy
  - Almost lethat side effect
  - 5 brain metastases → March 2019 no more options for treatmet

58 yo

MY HEALTH CAN'T WAIT

- **Create: Medical Institute of Advanced Oncology**

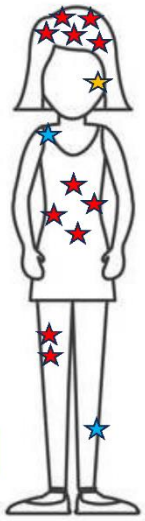
INMOA
INSTITUTO MÉDICO DE ONCOLOGÍA AVANZADA

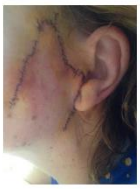
My mum:

- Diagnosed in December 2015
- 1st brain metastases june 2018
- Every six months new lesions...
  - 5 brain metastases, 1 in bowel 7cm length, leg, thorax...

RT + mEHT for 2 years (2019 to 2021)

RT + mEHT + low dose IT since January 2022 ...

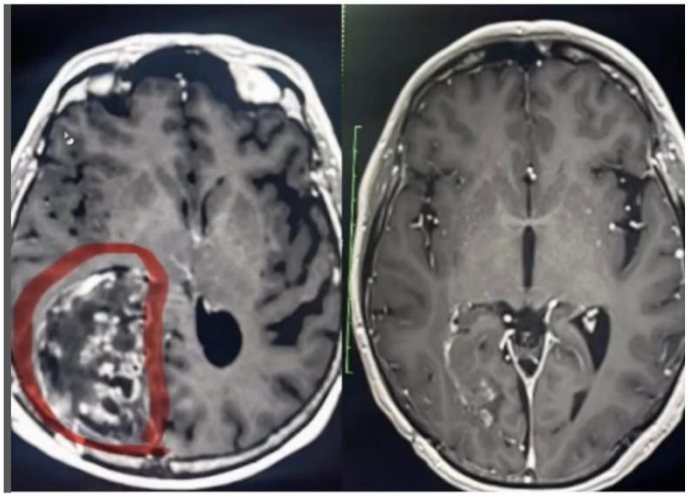




Metastases
Primary infiltrating melanoma
In situ melanoma

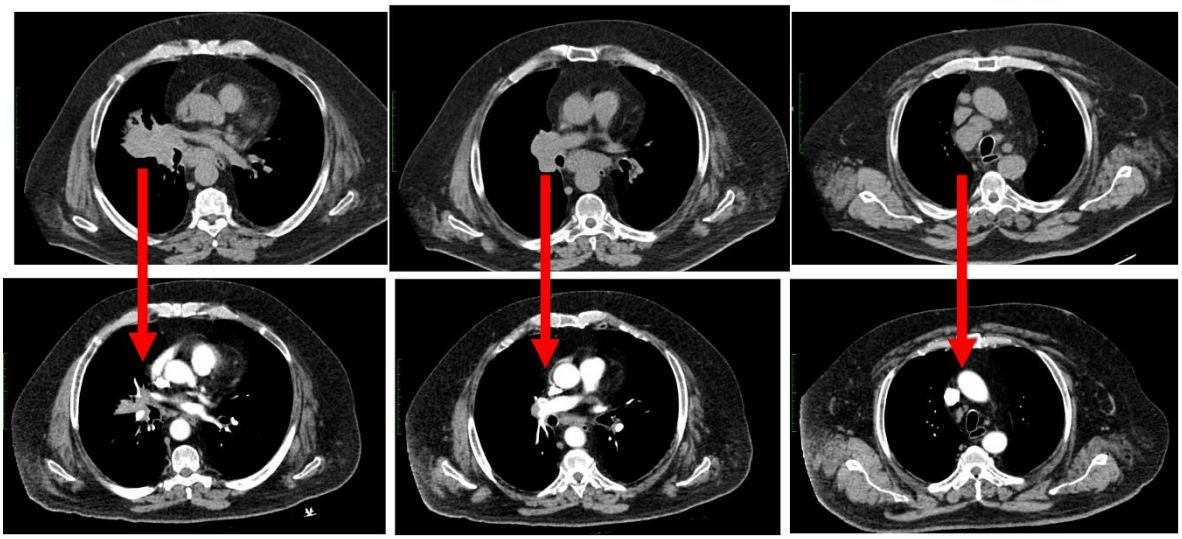
GBM treated with TMZ + mEHT
(18 treatments)

- Not candidate for surgery
- 10 months after treatment free of disease

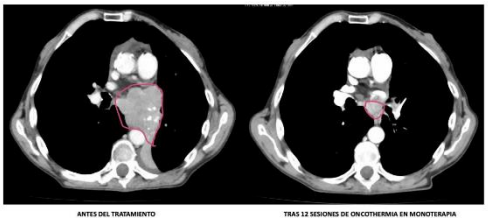


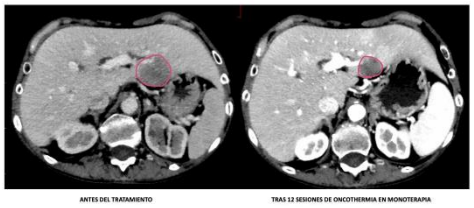
Microcitit lung cancer + Carboplatin-Etoposide
(12 mEHT treatments)

Male, 64 yo



Marina, Microcytic lung cancer with liver metastases

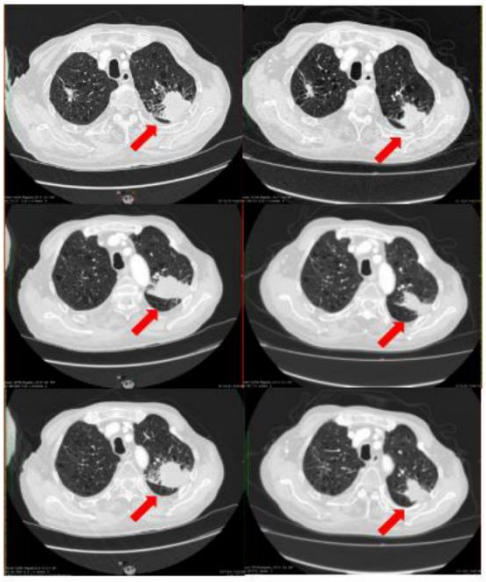




MONOTHERAPY

Not candidate for chemo/radiotherapy

BEFORE TREATMENT AFTER TREATMENT



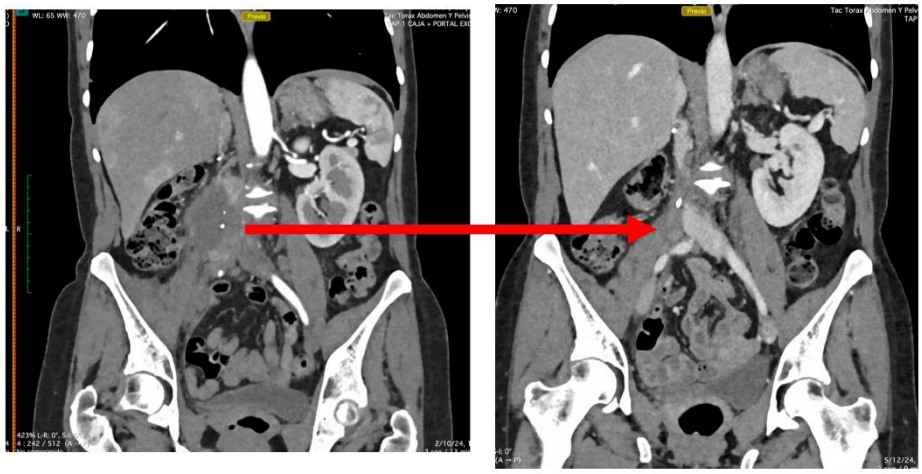
EPIDERMOID LUNG CANCER

12 mEHT treatments

MONOTHERAPY

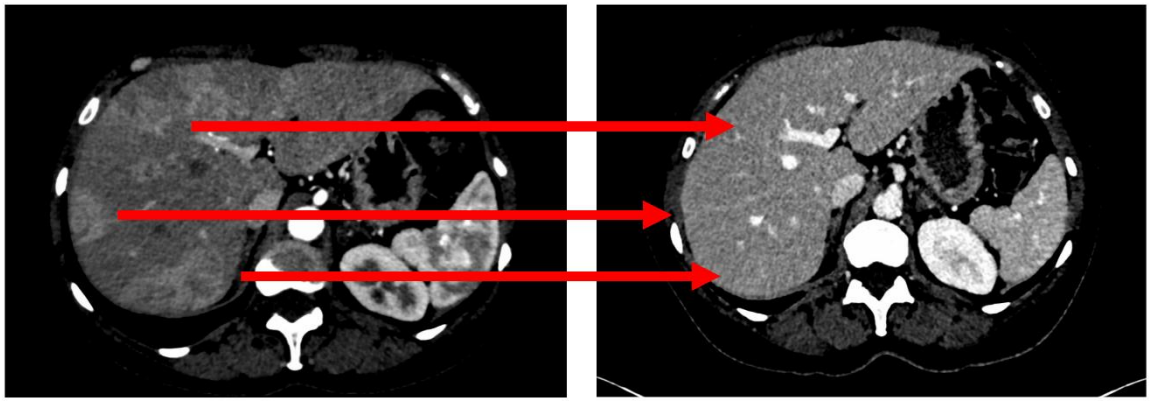
Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)

Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)

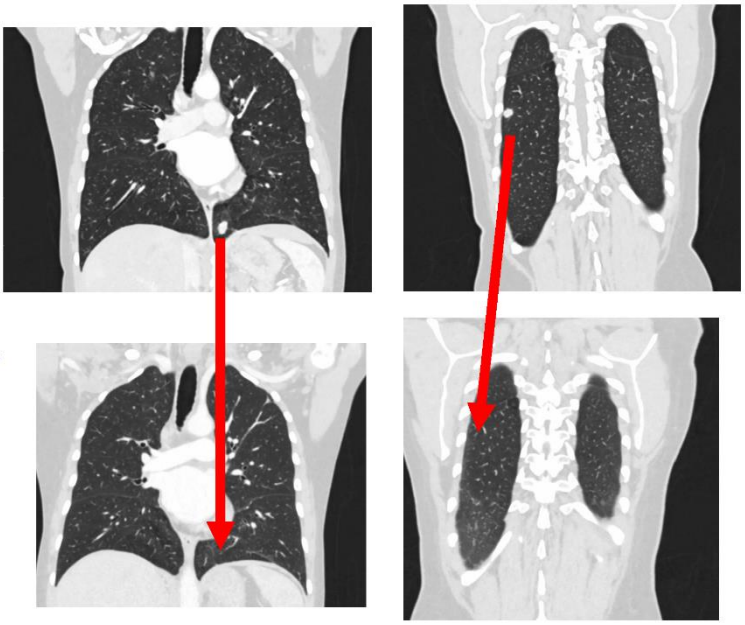


Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)

Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)



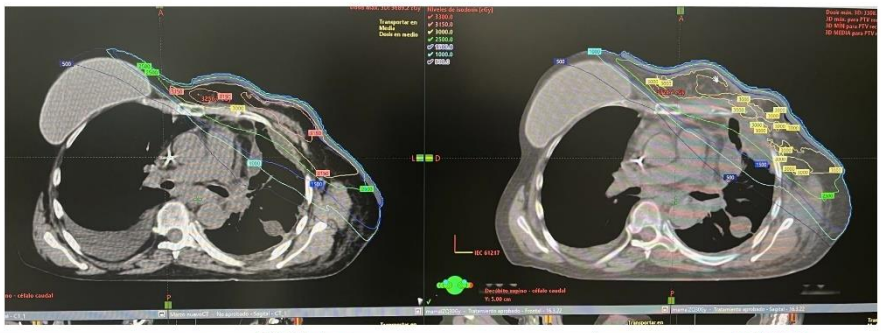
Female 53 yo, Renal cell cancer – stage IV (liver, lung, abdomen)
Cisplatin-Gemcitabine + mEHT (no tumor in 6 weeks)

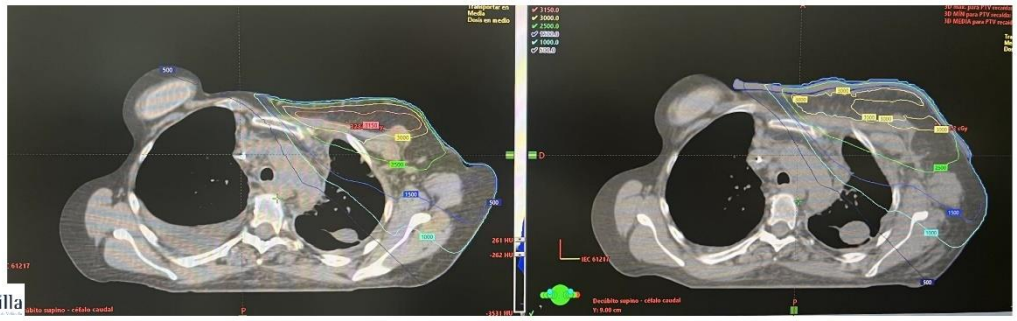


ABSCOPAL EFFECT

Breast Cancer

- No chemo
- 30 Gy





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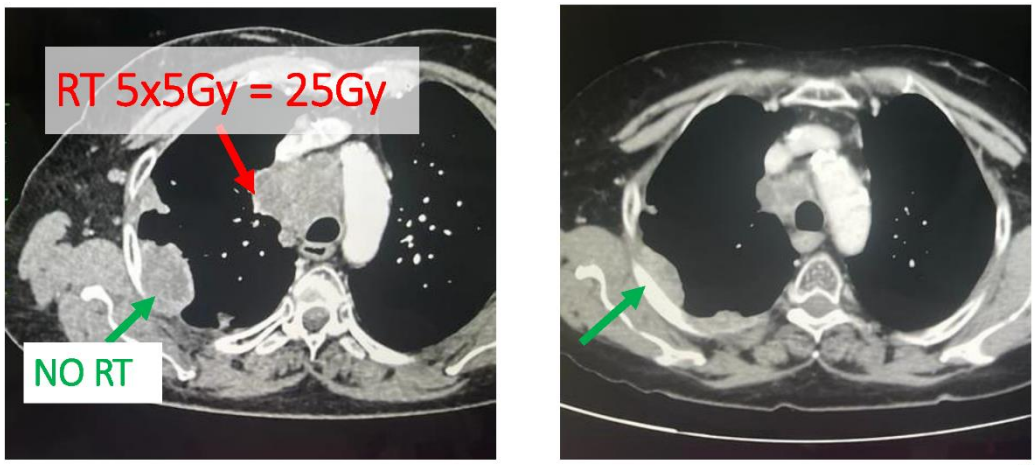
ABSCOPAL EFFECT - LUNG CANCER

Before treatment

2weeks after treatment

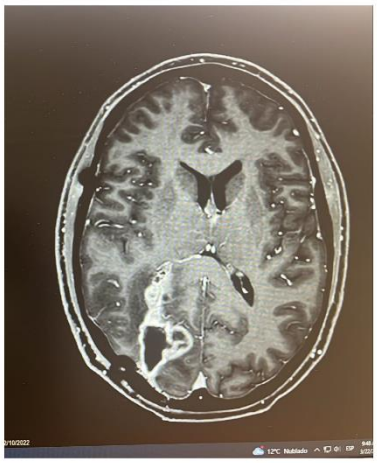


Thorax mEHT x 6

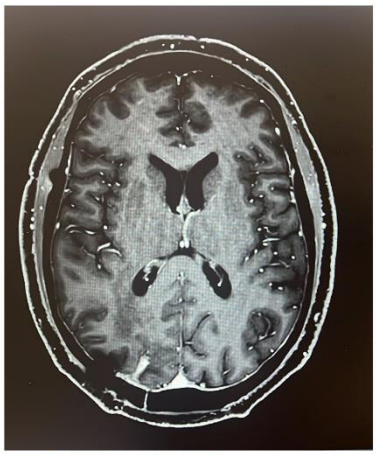
52 yo male, GBM IDH negative

Progressed 1 month after standard CT-RT

mEHT MONOTHERAPY

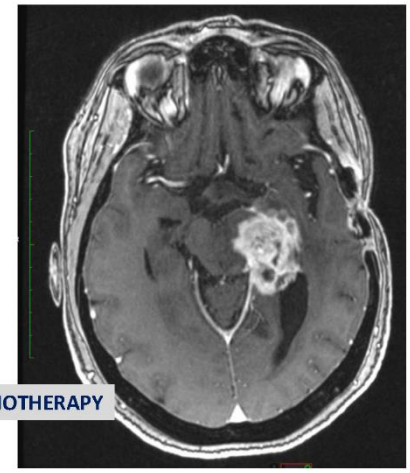


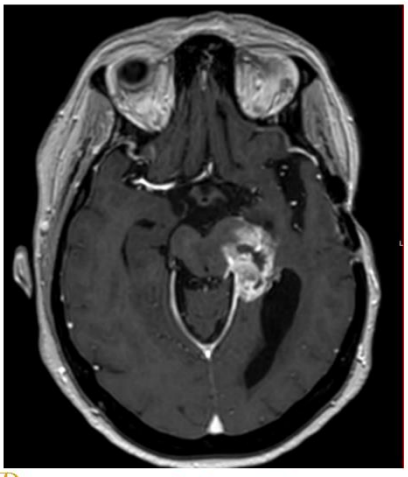
MRI after progression



MRI after 18 mEHT treatments

43 yo Female with "IDH –" GBM





mEHT MONOTHERAPY

MRI 1 month after mEHT treatment

5 years free of progression…

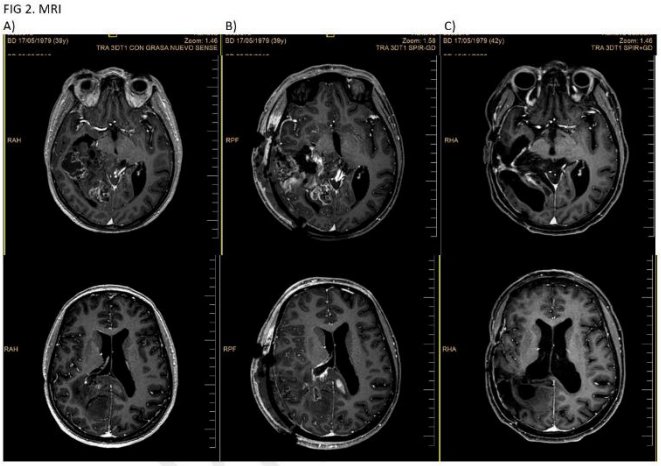
Grade II astrocitoma, female 37 yo. No complete surgery

RT 54Gy → Chemo PCV 6 months → **Progression after 3 months.**

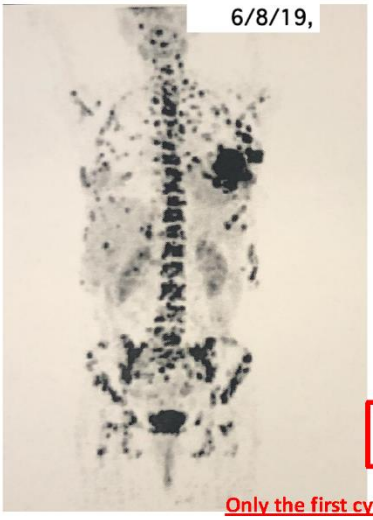
Partial surgery→ Not candidate chemo nor RT

mEHT MONOTHERAPY

FIG 2. MRI

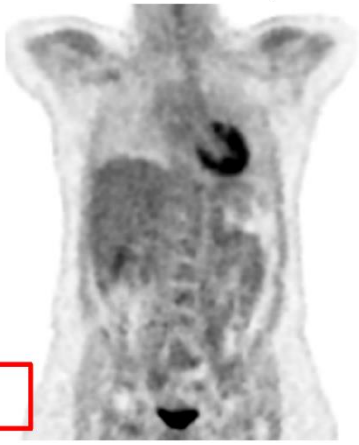


A) MRI at progression after surgery, radiotherapy and chemotherapy; B) MRI after second surger… (after progression); C) Last MRI 44 months after last surgery. Only mEHT performed from that tim…



6/8/19,

28/10/19,



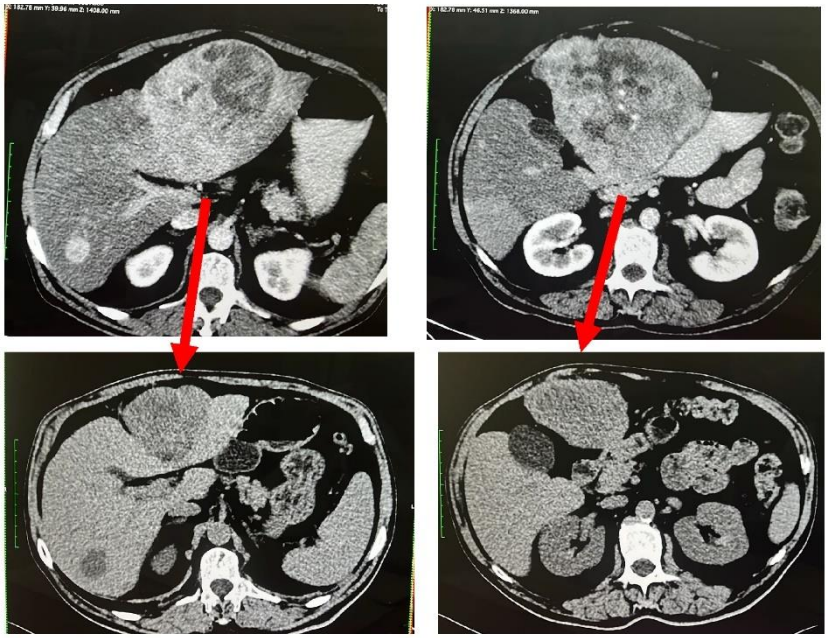
Breast cancer

4* CT cycles
29 mEHT treatments

2.5 months later
COMPLETE RESPONSE

Only the first cycle with paclitaxel + pertuzumab + trastuzumab.

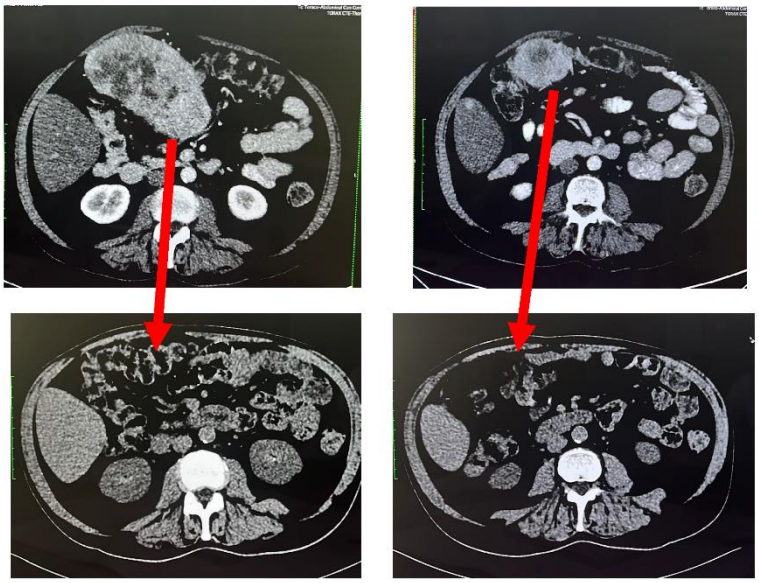
The other ones only pertuzumab + trastuzumab (patient desirees)



Stage IV hepatocarcinoma

Atezolizumab + mEHT

Results 2 months after treatment

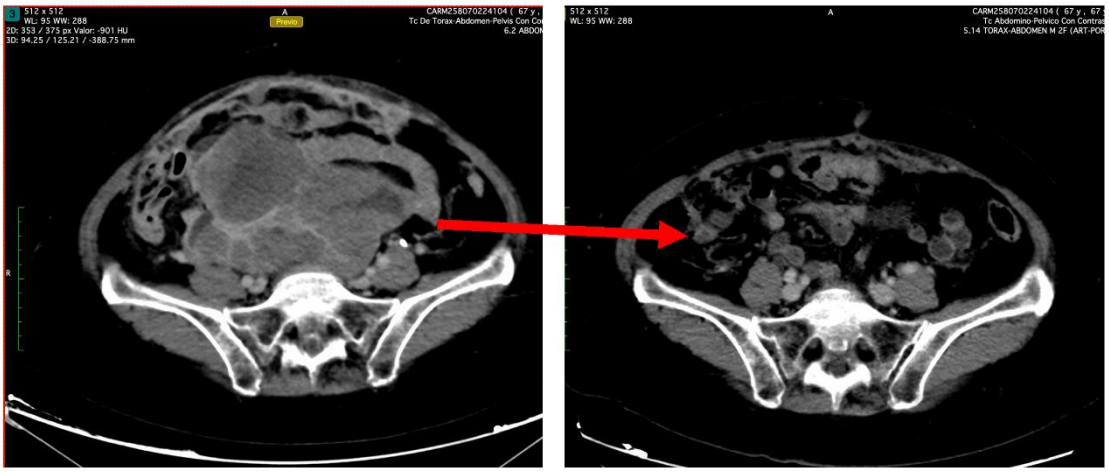


Stage IV
hepatocarcinoma

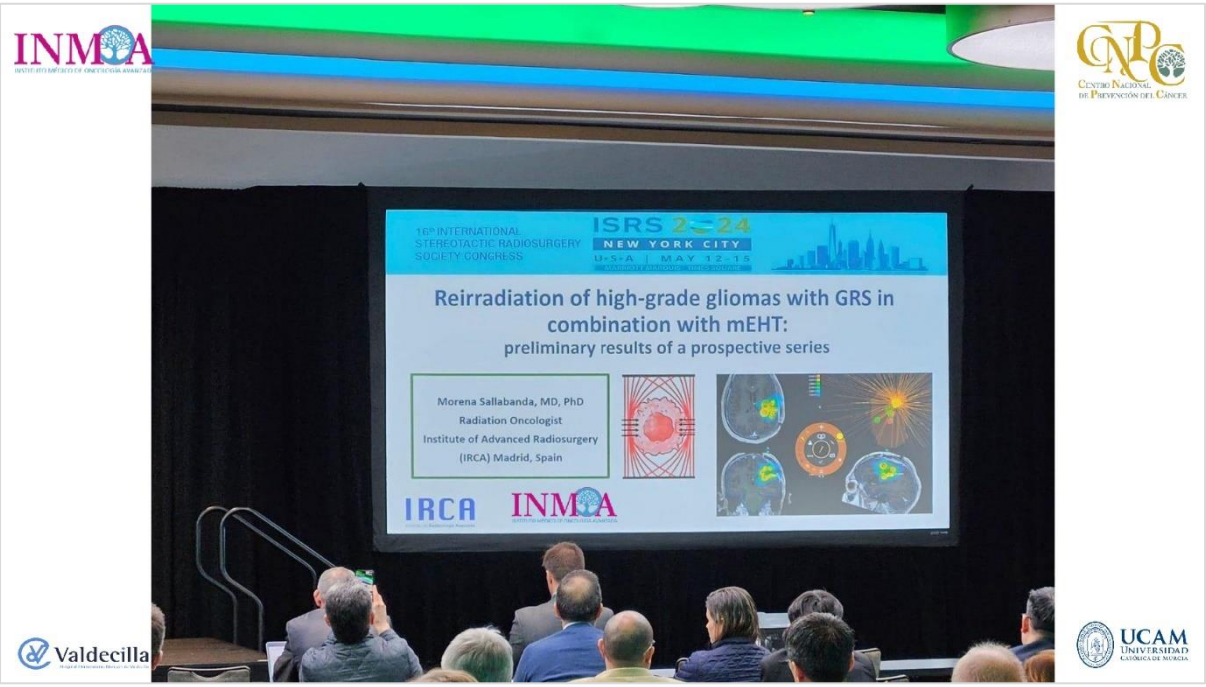
Atezolizumab + mEHT

Results 2 months after treatment

STAGE IV OVARIAN CANCER

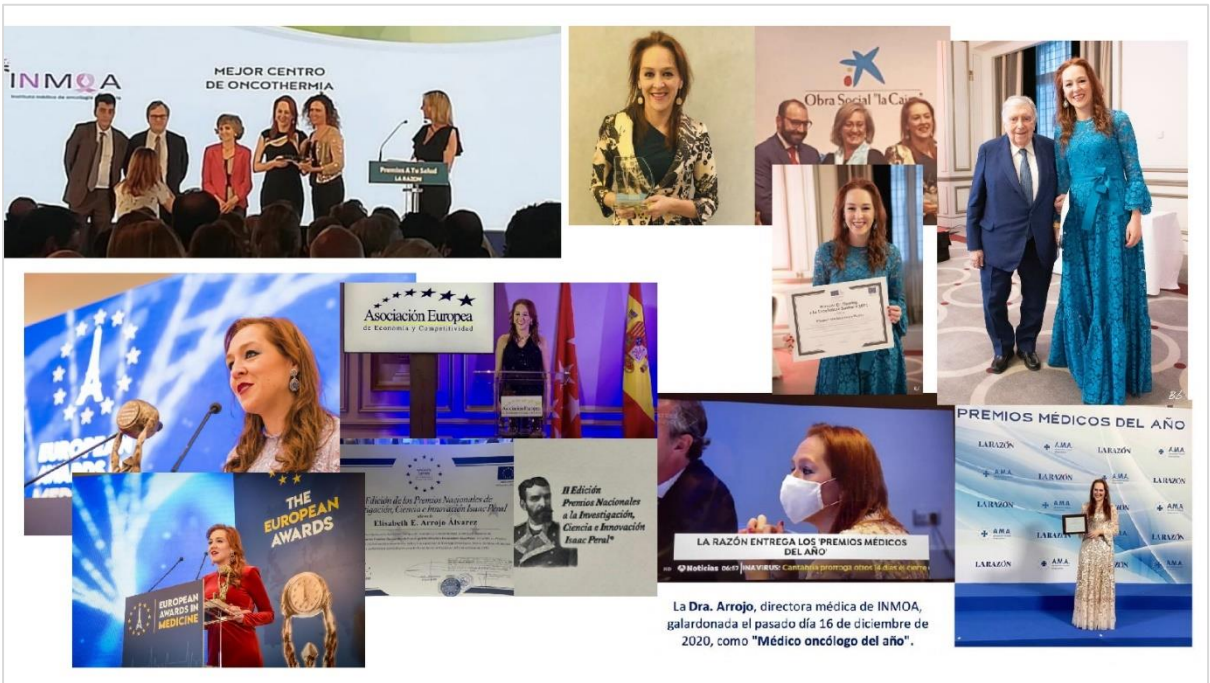


3 CT CYCLES (CARBOPLATIN + TAXOL) + 15 mEHT treatments


INMOA
16th INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY CONGRESS
ISRS 2024
NEW YORK CITY
U-S-A | MAY 12-15
Reirradiation of high-grade gliomas with GRS in combination with mEHT:
preliminary results of a prospective series
Morena Sallabanda, MD, PhD
Radiation Oncologist
Institute of Advanced Radiosurgery
(IRCA) Madrid, Spain
IRCA
INMOA
Valdecilla
UCAM


INMOA
My mum?
More than 6 years later...
THE EUROPEAN AWARDS
EUROPEAN AWARDS IN MEDICINE
Now:
- Alive
- No disease!!!
- No morbidities
Plaza
Dra. Elisabeth Arrojo
CORVERA
A Round square with my name...
2023
European Dr. Fleming Award


In less than 4 years...
INMOA
UCAM
>2000 sqf...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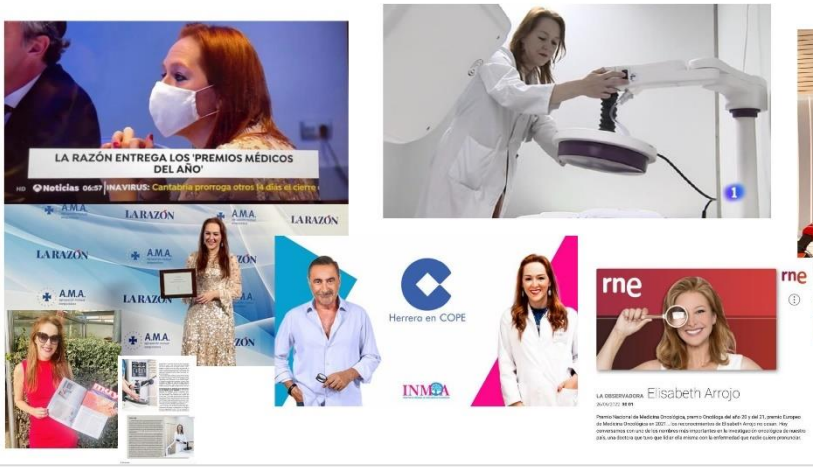
MEJOR CENTRO
DE ONCOTHERMIA
Obra Social "la Caixa"
Asociación Europea
de Economía y Competitividad
THE
EUROPEAN
AWARDS
EUROPEAN
AWARDS IN
MEDICINE
II Edición
Premios Nacionales
a la Investigación,
Ciencia e Innovación
Isaac Peral"
LA RAZÓN ENTREGA LOS 'PREMIOS MÉDICOS
DEL AÑO'
PREMIOS MÉDICOS DEL AÑO
La Dra. Arrojo, directora médica de INMOA,
galardonada el pasado día 16 de diciembre de
2020, como "Médico oncólogo del año".

INMOA in news...

News on TV...



A lot of interviews radio, newspapers, TV...

...

- INMOA, Madrid.
- INMOA, Vasque Country.

Murcia Catholic University


El Presidente y la Rectora de la
Universidad Católica San Antonio de Murcia

conforme a la propuesta formulada por el Excmo. Sr. Presidente de esta Universidad, y en virtud del acuerdo adoptado por su Consejo de Gobierno, en sesión celebrada el 20 de abril de 2022, se nombra a

Elisabeth Arroyo Álvarez

como

Catedrática Extraordinaria de Hipertermia Oncológica

y como prueba de ello, se expide el presente título acreditativo en Murcia, a 20 de abril de 2022.

El Presidente, La Rectora,

José Luis Mendoza Pérez — Josefina Gabriel Lozano

UCAM UNIVERSIDAD CATÓLICA DE MURCIA

First University Hyperthermia Professor

PRESENT/FUTURE...

cancers

MDPI

Review

Hyperthermia in Combination with Emerging Targeted and Immunotherapies as a New Approach in Cancer Treatment

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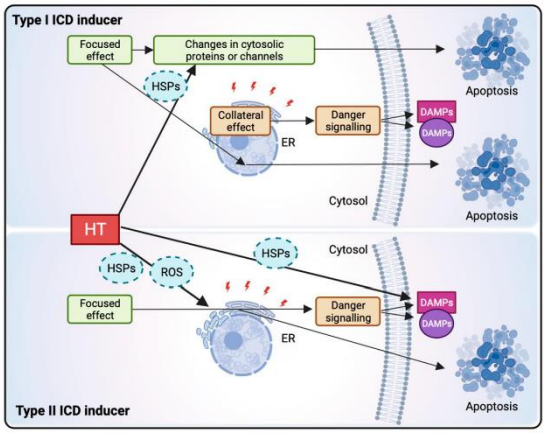

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Hyperthermia combined with immune checkpoint inhibitor therapy in the treatment of primary and metastatic tumors

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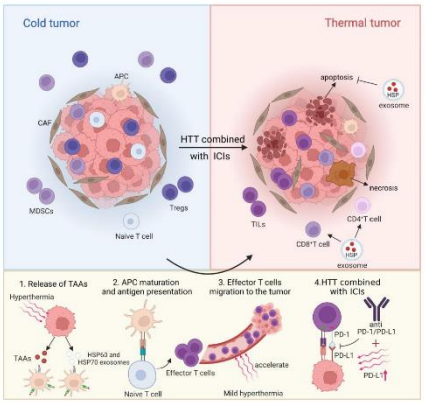

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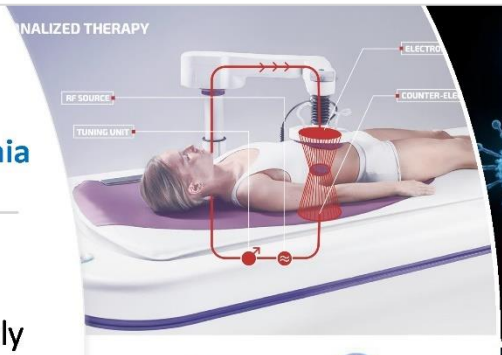
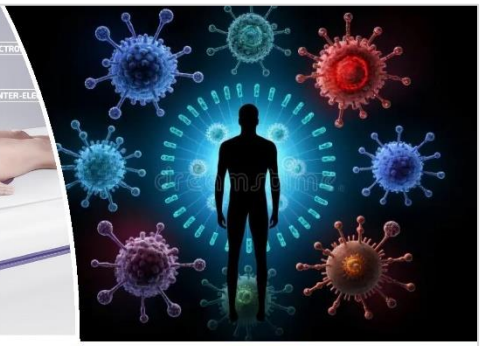
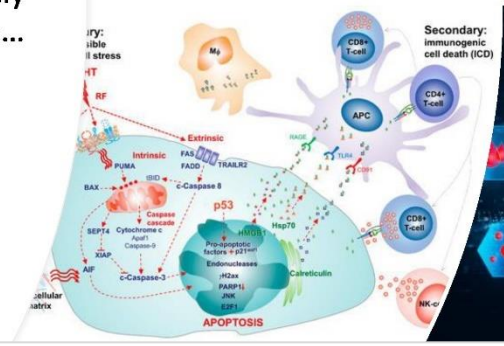
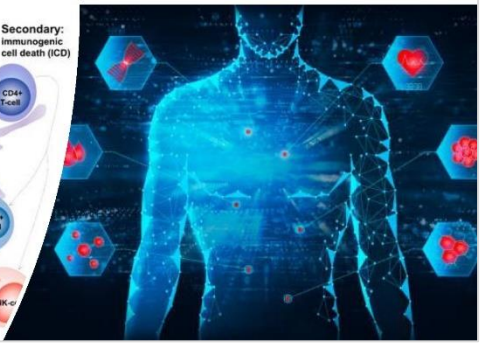
Modulated electrohyperthermia (mEHT)

More than only hyperthermia...









Conclusions

Scientifically Proven: Modulated electro-hyperthermia is supported by solid clinical and scientific evidence across various cancer types.

Treatment Amplifier: It significantly enhances the efficacy of both systemic therapies and radiotherapy, offering improved outcomes (From Good results to extraordinary...)

Standard of Care Potential: It deserves recognition and integration as a standard oncological treatment in multidisciplinary cancer care.

Immune system power: Its powerful immune-modulating effect opens a promising path for future research in cancer immunotherapy.